UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,963	02/08/2001	Beena Neelam	CL001112	5831

25748 7590 08/12/2004

CELERA GENOMICS CORP.
ATTN: WAYNE MONTGOMERY, VICE PRES, INTEL PROPERTY
45 WEST GUDE DRIVE
C2-4#20
ROCKVILLE, MD 20850

EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/778,963	Applicant(s) NEELAM ET AL.	
	Examiner Karen A Canella	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 4,8,9,13 and 24-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 26 is/are allowed.

6)☒ Claim(s) 4,8,9,13,24,25 and 27-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date March 3, 2003. + July 7, 2003
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgment is made of applicant's election with traverse of Group III claims 4-6, 8-11 and 22-23, drawn to nucleic acid molecules, vectors and host cells. The traversal is reference to claim 13, drawn to a method for detecting the nucleic acid of claim 14. Applicant argues that it would not be an undue burden in the examination process to include claim 13 with the elected Group III. It is noted that the restriction requirement was proper as s et forth in the previous Office action. However, in order to advance prosecution, claim 13 will be rejoined to the elected group, in light of the fact that all other claims were canceled.

2. Please note that a complete listing of the claims in the new format will be required in the response to this Office action even if no amendments are made to the claims. This is necessitated by the new format of IFW patent applications.

3. Claims 1-3, 5-7, 10-12 and 14-23 have been canceled. Claims 24-29 have been added. Claims 4, 8 and 13 have been amended. Claims 4, 8, 9, 13 and 24-29 are pending and examined on the merits.

Specification

4. The specification is objected to for failing to comply with the sequence requirements. Page 3, line 26 contains sequence disclosures that come within the definition of the Sequence Rules and Regulations.

Appropriate correction is required.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 12, line 30, and page 13, line 3 and line 21. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of making the host cell in vitro, does not reasonably provide enablement for methods of making the host cell in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 9 is drawn to a host cell containing the vector of claim 8. When given the broadest reasonable interpretation the host cell can be a recombinant cell in vitro or a recombinant cell in vivo. The specification contemplates the use of the disclosed nucleic acids for the construction of transgenic animals (page 37, lines 7-12) and in gene therapy in patients containing cells that are aberrant in Ras-like protein of the instant invention (page 43, lines 3-7). The specification is not enabling for using patients as host cells or for the construction of transgenic animals for the following reasons:

(A)As drawn to gene therapy

The instant specification does not teach how to overcome problems with in vivo delivery and expression with respect to the administration of the claimed nucleic acids or viral vectors comprising said nucleic acids. The state of the art is that in vivo gene delivery is not well developed and is highly unpredictable. For instance Verma et al (Nature, 1997, Vol. 389, pp. 239-242) teach that the Achilles heel of gene therapy is gene delivery. Verma et al state that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression (page 239, column 3). Eck et al (Gene-Based Therapy, In: The Pharmacological Basis of Therapeutics, Goodman and Gilman, Ed.s, 1996, pp. 77-101) teach that the fate of the DNA vector itself with regard to the volume of distribution, rate of clearance into tissues etc., the in vivo consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA the level of mRNA produced, the stability of the mRNA produced in vivo, the amount and stability of the protein produced and the proteins

compartmentalization or secretory fate within the cell are primary considerations regarding effective therapy. Eck et al state that these factors differ dramatically on the vector used, the protein being produced, and the disease being treated (Eck et al bridging pages 81-82).

As of the priority date sought, it was well known in the art how to infect or transfect cells in vitro or ex vivo with viral vectors. However, using viral vectors to deliver DNA to an organism in vivo, or using infected or transfected cells to deliver nucleic acids which encode a particular protein sequence to an organism in vivo is in the realm of gene therapy, and highly unpredictable in view of the complexity of in vivo systems. Orkin et al state ("Report and Recommendation of the Panel to Assess the NIH Investment in Research on Gene Therapy", NIH, 1995) that clinical efficacy had not been definitively demonstrated with any gene therapy protocol (page 1, second paragraph). Orkin et al defines gene therapy as the transfer of DNA into recipient cells either ex vivo or in vivo (page 7, under the heading "Gene transfer"), thus encompassing the instant claims drawn to the administration of antigen presenting cells transfected or infected ex vivo. Orkin et al concludes that, "none of the available vector systems is entirely satisfactory, and many f the perceived advantages of vector systems have not been experimentally validated. Until progress is made in thee areas, slow and erratic success in applying gene transfer methods to patients can be expected" Orkin et al comment that direct administration of DNA or DNA in liposomes is not well developed and hindered by the low efficiency of gene transfer (page 8, paragraph 5). Orkin et al teach that adequate expression of the transferred genes is essential for therapy, but that the level and consistency of expression of transferred genes in animal models was unknown. Orkin et al states that in protocols not involving ex vivo infections/transfection, it is necessary to target the expression of the transferred genes to the appropriate tissue or cell type by means of regulatory sequences in gene transfer vectors. The specification does not teach a vector having a specific regulatory sequence which would direct the expression of the nucleic acids within the appropriate tissue type.

The specification does not remedy any of the deficiencies or the prior art with regard to gene therapy. Given the lack of any guidance from the specification on any of the above issues pointed out by Verma or Eck or Orkin. One of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the methods of claims.

(B)As drawn to a transgenic animals

The specification does not provide guidance in the making of a transgenic animal comprising the instant recombinant polynucleotides or transformed cells. In the art of producing transgenic animals, the phenotype of the resultant transgenic animal is not always predicable or viable. The vectors to be used for directing the expression of transgenes in a given tissue or in all tissues must contain the appropriate regulatory regions (Houdebine, Journal of Biotechnology, 1994, Vol. 34, pp. 269-287, see bridging pages 272-273) and expression is heavily dependent on the site of integration in the host genome, and the site of integration is presently unpredictable (Houdebine, page 277, column 1). Therefore, it is concluded that one of skill in the art would undergo undue experimentation in order to make the instant recombinant polynucleotides and cells within a transgenic animal.

Amendment of the claims to recite both "isolated vector" and "isolated host cell" would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 8, 9, 13, 24, 25 and 27-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Cismowski et al (WO 99/58670, reference of the IDS filed March 4, 2003).

Claim 4 is drawn in part to an isolated nucleic acid molecule consisting of a nucleotide sequence selected from the group consisting of a nucleotide sequence that encodes a protein comprising the amino acid sequence of SEQ ID NO:2; a nucleotide sequence consisting of SEQ ID NO:1 and a nucleotide sequence that is completely complementary to the aforesaid nucleotide sequences. Claim 8 is drawn to a nucleic acid vector comprising a nucleotide sequence of claim 4. Claim 9 is drawn to a host cell containing the vector of claim 8. Claim 24 is drawn to a process for producing a polypeptide comprising culturing the host cell of claim 9 under conditions sufficient for the production of said polypeptide and recovering said polypeptide form

the host cell culture. Claim 25 is drawn to an isolated polynucleotide consisting of SEQ ID NO:1. Claim 27 embodies the vector of claim 8, wherein said vector is selected from the group consisting of a plasmid, virus and bacteriophage. Claim 28 embodies the vector of claim 8 wherein said isolated nuclei acid molecule is inserted into said vector I proper orientation and correct reading frame such that the protein of SEQ ID NO:2 may be expressed by a cell transformed with said vector. Claim 29 embodies the vector of claim 8 wherein said isolated nucleic acid molecule is operatively linked to a promoter sequence.

Claim 13 is drawn to a method of detecting the presence of a nucleic acid sequence of claim 4 in a sample comprising contacting the sample with an oligonucleotide comprising at least 20 contiguous nucleotides that hybridize to said nuclei acid molecule under stringent conditions and determining whether the oligonucleotide binds to said nucleic acid molecule in the sample.

Cismowski et al disclose the isolated nucleic acid of SEQ ID NO:1 with the exception of a substitution of a G nucleotide for a C nucleotide at position 533. Cismowski et al disclose the isolated nucleic acid encoding SEQ ID NO:2 with the exception of X at position 166 in place of Serine. Cisnowski et al disclose that the nucleic acids of the invention encode a AGS protein having at least 86% sequence identity to SEQ ID NO:1 and isolated nucleic acid encoding proteins having an amino acid sequence at least 97% identical to SEQ ID NO:2 (page 3, lines 5-21). Cismowski et al specifically disclose a vector selected from a plasmid, virus (page 20, lines 11-29) or bacteriophage (page 27, lines 19-20), thus fulfilling the specific embodiments of claim 27. The instant SEQ ID NO:1 and 2 are 99% identical to SEQ ID NO:1 and encode a protein 99% identical to SEQ ID NO:2. Cismowski et al disclose that DNA sequence polymorphisms that lead to changes in the amino acid sequence of AGS may exist within a population (page 13, lines 1-4). Cismowski et al disclose that the invention comprises host cells and vectors comprising said isolated nucleic acids and methods of producing recombinant proteins comprising the culturing of host cells which express the recombinant nucleic acid (page 3, lines 24-26). Cismowski et al disclose a method for detecting AGS in a sample comprising a labeled nucleic acid probe capable of hybridizing to AGS mRNA, wherein the probe can be an oligonucleotide of at least 30 nucleotides in length which hybridize under stringent conditions to AGS mRNA (page 66, lines 8-16), thus fulfilling the specific embodiment of claim 13 which specifies a probe of at least 20 nucleotides.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
8/9/2004